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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/552,696	07/13/2006	Darren Magda	25922-710.831	3832

21971 7590 11/02/2007

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EXAMINER	
JARRELL, NOBLE E	

ART UNIT	PAPER NUMBER
1624	

MAIL DATE	DELIVERY MODE
11/02/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/552,696	MAGDA, DARREN	
	Examiner	Art Unit	
	Noble Jarrell	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *06 October 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/16/2006;11/30/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Current Status of 10/552696

1. Claims 1-22 are pending in the instant application and are being examined in the current office action.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the preparation of compounds of claims 1-10 and their respective salts, does not reasonably provide enablement for prodrugs of compounds of claims 1-10. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

While applicants adequately show the preparation of examples 1-44 and their salts, the preparation of prodrugs of these compounds is not shown. The development of prodrugs requires an extensive undertaking because the correct chemical modification must be found. In addition, once a prodrug is found, it is considered a new drug entity and thus requires extensive and costly studies to determine safety and efficacy (Jantzen and Robinson, *Modern Pharmaceutics*, Gilbert Banker, editor, **1996**, pg 596).

> The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in Wands states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2sd 1404). Clearly, enablement

of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Consideration of the relevant factors sufficient to establish a *prima facie* case for lack of enablement is set forth herein below:

(1) The nature of the invention and (2) the breadth of the claims:

The claims are drawn to sapphyrin derivatives.

(3) The state of the prior art and (4) the predictability or unpredictability of the art:

Jantzen and Robinson show that development of a prodrug requires extensive experimentation in the determination of the correct chemical modification, safety, and efficacy.

(5) The relative skill of those in the art:

One of ordinary skill in the art is familiar with the synthetic techniques relied upon to make examples 1-44.

(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:

The specification has provided guidance for preparation of parent compounds of claims 1-10.

However, the specification does not provide guidance for preparation of prodrugs.

(8) The quantity of experimentation necessary:

Considering the state of the art as discussed by the references above, particularly with regards to claims 1-22 and the high unpredictability in the art as evidenced therein, and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate in the scope of the claims.

4. Claims 17-22 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of lung cancer and lymphomas, does not reasonably provide enablement for all types of cancers. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Applicants show that the examples prepared can effectively inhibit tumor growth in the A549 cell line (page 30) and in lymphomas (page 32). However cancer is more than one disease ("Cancer definition", http://www.medterms.com/script/main/art.asp?articlekey=2580, accessed October 18, 2007). Applicants only show treatment of two diseases, lung cancer and lymphatic cancer. Currently, the claims are drawn to treatment of any neoplasm.

> The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in Wands states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2sd 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Consideration of the relevant factors sufficient to establish a *prima facie* case for lack of enablement is set forth herein below:

(1) The nature of the invention and (2) the breadth of the claims:

The claims are drawn to treating neoplasms with sapphyrins..

(3) The state of the prior art and (4) the predictability or unpredictability of the art:

Cancer is not just one disease, but a variety of diseases.

(5) The relative skill of those in the art:

One of ordinary skill in the art can replicate the tests used for tumor inhibition described in the specification

(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:

The specification has provided guidance for treatment of lung cancer and lymphatic cancer.

However, the specification does not provide guidance for the treatment of all cancers..

(8) The quantity of experimentation necessary:

Considering the state of the art as discussed by the references above, particularly with regards to claims 17-22 and the high unpredictability in the art as evidenced therein, and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate in the scope of the claims.

Claim Rejections - 35 USC § 102

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Shevechuk et al. (*Tetrahedron Letters*, **2001**, *42*, 2447-50, included in IDS). Shevechuk et al. report compounds 6 through 9 on page 2447. Compound 6 anticipates claim 1 because the variables have the following meanings: R^1 and R^8, $(CH_2)_4$-OH; R^2-R^7, Methyl; and R^9 an R^{10} are ethyl. In compound 7, variables R^3-R^6 are O-Me (O-Ak), and the other variables have the same meanings as they do in compound 6. In compound 8, variables R^3-R^6 are ethyl, and the other variables have the same meanings as they do in compound 6. In compound 10, variables R^3-R^6 are ethyl and variables R^1 and R^8 are $(CH_2)_3CH_3$. Thus claim 1 is rejected by these four structures.

6. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Shionoya et al. (*Journal of the American Chemical Society*, **1992**, *114*, 5714-22, included in IDS). Compound H_3SAP 1 on page 5715 anticipates claim 1 because variables R^2, R^4, R^5, and R^7 are methyl and variables R^1, R^3, R^6, R^8, R^9, R^{10} are ethyl. Thus, claim 1 is anticipated.

7. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Sessler et al. (*Accounts of Chemical Research*, **2001**, *34*, 989-97, included in IDS). Sessler et al. report four structures (sapphyrin, compound 4, compound 14, and compound 25). In sapphyrin (pg 989), each of the variables is hydrogen. In compound 4 (pg. 990), variables R^1, R^4, R^5, and R^8 through R10 are methyl and variables R^2, R^3, R^6, and R^7 are ethyl. In compound 14 (pg. 990), all of the variables have the same meanings as compound 4, but variables R^2, R^3, R^6, R^7, R^9, and R^{10} are ethyl. In compound 25, variables R^3-R^6 and R^9-R^{10} are ethyl, R^2 and R^7 are methyl, and R^1 and R^8 are each $(CH_2)_4$-OH.

8. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Malya et al. (*Journal of Physical Chemistry*, **1990**, *94*, 3597-3601). Figure 1 on page 3598 anticipates claim 1 because variables R^2, R^4, R^5, and R^7 are methyl and R^1, R^3, R^6, R^8, R^9, and R^{10} are ethyl.

9. Claims 1, 11, and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Sessler et al. (US 5543514, issued August 6, 1996, included in IDS). Sessler et al. report compound A2 of table 2, where variables R^2, R^4, R^5, and R^7 are methyl, R^3, R^6, R^9, and R^{10} are ethyl, and R^1 and R^8 are $(CH_2)_4$-OH. Claim 11 is anticipated because pharmaceutical compositions of these compounds are taught (column 18, lines 34-44). Claim 17 is anticipated because these compounds are being used to treat cancer (column 18, lines 42-55).

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

12. Claims 1 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sessler et al. (*Accounts of Chemical Research* article cited in 102(b) rejection). Sessler et al. teach compound 34 on page 993, where variables R^1 and R^8 are $(CH_2)_2C(O)N((CH_2)2\text{-}OH)_2$, R^2, R^4, and R^7 are methyl, and variables R^3, R^6, and R^9-R^{10} are ethyl. Although compound 34 does not directly anticipate compounds of claims 1 and 7 There is no ether linkage between the alkyl group and the carbonyl group), it shown that compound 34 binds DNA (page 995). Addition of compound 34 to double-stranded DNA leads to an immediate precipitation of green (sapphyrin laden) fibers, which shows that there is a strong interaction between DNA and compound 34. As a result of this finding compound 34 could be used for antisense or antigene therapy Claims 1 and 7 are rendered obvious because variable R^{31} and R^{32} can both be $(CH_2)_2$-OH. It would be obvious to try compound 34 in place of a compound of claim 7 in gene therapy based on the findings of Sessler et al.

Allowable Subject Matter

13. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Noble Jarrell whose telephone number is (571) 272-9077. The examiner can normally be reached on M-F 7:30 A.M - 6:00 P.M. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson can be reached on (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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